peripheral blood flow cytometry (human CD45/mouse CD45). The docetaxel-treated group showed the longest survival, outperforming vincristine, a drug of standard pediatric ALL therapy, demonstrating that docetaxel can be therapeutically superior in a functionally selected subgroup. Similarly, we identified patients who were functionally resistant to cytarabine (standard chemotherapy) but sensitive to clofarabine. In vivo validation in PDX models confirmed improved survival in the clofarabine-treated group compared to the cytarabine-treated group, consistent with ex vivo functional predictions. Previous clinical trials evaluating docetaxel or the substitution of cytarabine with clofarabine in pediatric ALL failed to demonstrate population-level benefit, leading to the rejection of these strategies. Our data suggest that these negative outcomes may reflect the lack of functional patient stratification, whereby true responder subpopulations are diluted within unselected cohorts. We conclude that ex vivo functional drug screening enables the identification of biologically defined responder subgroups, redefining clinical trial randomization as a biologically driven process. This approach has the potential to reshape clinical trial design, optimize drug development, and establish a truly functional precision medicine framework in pediatric oncology.

Keywords: Functional precision medicine, Ex vivo drug screening, Pediatric acute lymphoblastic leukemia, Patient stratification, Clinical trial redesign.

Conflicts of interest: The authors declare that they have no conflicts of interest.

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RADIOLABELING AND BIODISTRIBUTION OF [^{68}GA]GA-FAPI-46 IN A HUMAN NON-SMALL CELL LUNG CANCER XENOGRAFT MODEL

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Introduction: Fibroblast Activation Protein (FAP) is a transmembrane protein overexpressed in cancer-associated fibroblasts within the tumor microenvironment of several solid tumors. Due to its selective expression, FAP has become an attractive molecular target, leading to the development of high-affinity inhibitors such as FAPi-46. When conjugated with DOTA, FAPi-46 can be radiolabeled with gallium-68, enabling tumor imaging by PET/CT. The development of the radiolabeling process and the evaluation of biodistribution parameters in animal models is an essential step in translational research for the successful implementation of this radiopharmaceutical in routine clinical practice. **Objectives:** To describe preliminary results of the radiolabeling of FAPi-46 and biodistribution in animal model of non-small cell lung cancer (NSCLC). **Materials and Methods:** [68Ga]GaCl3 was eluted from generator (68Ge/68Ga) with 6mL of 0.1M HCl and trapped on an SCXcartridge. The radionuclide was subsequently eluted with 0.5mL of a 5M NaCl/5.5N HCl solution (95:5, v/v) into a reaction vial containing 50μg of FAPi-46 dissolved in 1.5mL of acetate buffer (pH 4.5), 0.1mL of ethanol and 0.1mL of ascorbic acid (10mg/mL). The reaction mixture was heated at 95°C/15min. The product was purified using Sep-Pak C18 cartridge, preconditioned with EtOH and saline, eluted with 70% ethanol, sterile-filtered through a 0.22μm filter, and finally diluted with 6mL of saline. For biodistribution studies (CEUA-6249), male Balb/c nude mice (~25g) were allocated into three groups: healthy controls (n=5) and tumor-bearing animals evaluated at 30 and 60 min post-injection (n=6/group). Tumors were induced by (sc) inoculation of 100 μL containing 5 $\times$ 10^6 A-549 cells in matrigel into right thigh, with tumor growth observed after 4–5 weeks. Animals received an activity ranging from 4.8–6.6 MBq. At the selected time points, organs were harvested, weighed, and measured using a gamma-counter. Results were expressed as mean % injected dose per gram of tissue (%ID/g). Additionally, values were normalized to allow relative comparison among organs, assuming the sum of all measured %ID/g as 100%. Analyzed tissues included blood, heart, spleen, liver, stomach, intestines, lungs, kidneys, tumor, contralateral muscle, and carcass. Tumor-to-kidney and tumor-to-muscle uptake ratios were calculated. **Results:** In healthy controls, the highest uptake was observed in kidneys (38.61%ID/g), followed by intestines (15.11%ID/g) and stomach (13.02%ID/g). In tumor-bearing animals at 30min post-injection, tumor uptake reached 18.52%ID/g, with concurrent distribution in kidneys (28.92%ID/g), lungs (8.36%ID/g), blood (7.09%ID/g), and muscle (2.15%ID/g). At 60min, tumor uptake was 15.40%ID/g, while kidneys, intestines, blood, and muscle presented values of 15.15%ID/g, 24.38%ID/g, 4.91%ID/g, and 3.18%ID/g, respectively. Tumor-to-background ratios reflected this distribution pattern: at 30min, tumor-to-muscle and tumor-to-blood ratios were 8.56±2.32 and 2.67±1.00; at 60min, these ratios were 5.58±2.01 and 3.26±1.09. **Conclusion:** These findings indicate that although absolute tumor uptake decreases over time, tumor-to-blood contrast improves at later time points, supporting favorable imaging properties. Overall, the data demonstrate rapid systemic clearance, sustained tumor retention, and high tumor-to-background contrast, suggesting that [68Ga]Ga-FAPi-46 is a promising PET-tracer for tumors image, including NSCLC.

Keywords: Positron-emission tomography, Radiopharmaceuticals, Fibroblast activation protein, Gallium radioisotopes, Models, Animal.

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EVALUATION OF NEW RADIOLABELED ANTI-EGFR PEPTIDE MODIFIED BY BIS (SEMICARBAZONE) METAL CHELATOR AS THERANOSTIC STRATEGY IN COLORECTAL AND HEAD AND NECK CANCERS

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Introduction: Colorectal cancer (CRC) and head and neck squamous cell carcinoma (HNSCC) remain major challenges in oncology due to their high incidence, aggressive behavior, and frequent resistance to targeted therapies. Dysregulation of the epidermal growth factor receptor (EGFR) signaling pathway is a common molecular hallmark of both malignancies and is strongly associated with poor prognosis. Although anti-EGFR therapies are clinically available, their efficacy is limited by intrinsic and acquired resistance mechanisms, including RAS mutations in CRC and activation of alternative signaling pathways in HNSCC. These limitations highlight the need for innovative strategies that combine precise molecular targeting with alternative mechanisms of tumor control. In this context, nuclear medicine theranostics, integrating diagnosis and therapy within a single molecular platform, represents a promising approach. **Objectives:** This study aims to evaluate, in preclinical models, a novel radiolabeled anti-EGFR peptide (coded for intellectual property protection) conjugated to a bis(semicarbazone) metal chelator as a potential theranostic agent for colorectal and head and neck cancers. **Materials and Methods:** A bis(semicarbazone)-based bifunctional chelator was synthesized and conjugated to a coded anti-EGFR peptide, enabling stable coordination with diagnostic (68Ga) and therapeutic (67Cu/64Cu) radionuclides. The resulting compound will be characterized in terms of radiochemical purity and stability. In vitro studies will be conducted using EGFR-positive CRC and HNSCC cell lines, employing both two-dimensional cultures and three-dimensional spheroid models to evaluate binding specificity, internalization, cytotoxicity, and mechanisms of cell death. Molecular effects on proliferative and apoptotic signaling pathways will be investigated. In vivo experiments will include biodistribution, acute toxicity, and imaging evaluation by micro-PET/SPECT/CT in healthy mice and tumor-bearing xenograft models, as well as assessment of antitumor efficacy in therapeutic settings. **Results (Expected):** It is expected that the radiolabeled peptide–chelator conjugate will demonstrate high radiochemical stability and selective interaction with EGFR-overexpressing tumor cells. In vitro assays are anticipated to show efficient tumor targeting, adequate penetration in three-dimensional tumor models, and induction of tumor cell death through radiation-mediated mechanisms. In vivo studies are expected to reveal favorable pharmacokinetic profiles, enhanced tumor uptake, limited nonspecific accumulation, and acceptable safety margins. **Conclusion:** This project is expected to generate robust preclinical evidence supporting the use of a bis(semicarbazone)-modified, radiolabeled anti-EGFR peptide as an innovative theranostic platform for colorectal and head and neck cancers. The proposed strategy may contribute to improved patient stratification, high-contrast molecular imaging, and the development of targeted radiotherapeutic approaches, addressing key limitations of current EGFR-directed treatments.

Keywords: Colorectal cancer, Head and neck cancer, EGFR, Radiolabeled peptides, Theranostics.

Conflicts of interest: Not declared.

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LIPOSOMAL NANOFORMULATION OF A COPPER-BASED COMPLEX ASSOCIATED WITH PARPI MODULATES ANGIOGENIC PROCESSES IN ENDOTHELIAL CELLS

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Angiogenesis is a highly regulated process and essential for the progression of solid tumors, as it ensures the continuous supply of oxygen and nutrients to metabolically dysregulated cells. This process involves degradation of the basement membrane, activation, proliferation, and migration of endothelial cells and is controlled by a balance between pro- and antiangiogenic factors, which is frequently disrupted in